Paper No. __

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte THIERRY BOON-FALLEUR, PIERRE VAN DER BRUGGEN, BENOIT VAN DEN EYNDE, ALINE VAN PEL, ETIENE DE PLAEN, CHRISTOPHE LURQUIN, PATRICK CHOMEZ and CATIA TRAVERSARI

Appeal No. 2006-0956
Application No. 08/819,669[1]

ON BRIEF

Before GRON, LANE and GRIMES, Administrative Patent Judges.

GRON, Administrative Patent Judge.

DECISION ON APPEAL UNDER 35 U.S.C. § 134

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[1] Application for patent filed March 17, 1997. According to applicant, this application is a divisional of Application 08/142,368, filed May 2, 1994, now U.S. Patent 5,925,729, issued July 20, 1999; which is a continuation-in-part of Application 07/807,043, filed December 12, 1991, now U.S. Patent 5,342,774, issued August 30, 1994; which is a continuation-in-part of Application 07/764,365, filed September 23, 1991, abandoned; which is a continuation-in-part of Application 07/728,838, filed July 9, 1991, abandoned; which is a continuation-in-part of Application 07/705,702, filed May 23, 1991, abandoned.

Introduction

This is an appeal under 35 U.S.C. § 134 from an examiner's final rejections of Claims 183-191, all claims pending in Application 08/819,669, filed March 17, 1997. All pending claims stand finally rejected under 35 U.S.C. § 112, first paragraph, as supported by a specification which, as filed, would not have provided an adequate written description of the full scope of the subject matter claimed, and/or would not have enabled persons skilled in the art to make and use the full scope of the subject matter claimed without undue experimentation.

A. Grouping of claims

According to appellant's Brief on Appeal (BA), Claims 183-191 do not stand or fall together (BA 5). Appellant grouped Claims 183, 185, 186, 188, 189 and 191 together and grouped Claims 184, 187 and 190 separately (BA 5). The Examiner's Answer (EA) acknowledges that dependent Claims 184, 187, and 190 further limit the tumor rejection antigen precursors of Claims 183, 185, 186, 188, 189 and 191 to ones comprising "the amino acid sequence set forth in SEQ ID NO: 26, a tumor rejection antigen associated with MAGE-1" (EA 3). In his Examiner's Answer, the examiner first established a third claim grouping of Claims 189-191 which depend respectively from composition Claims 186-188 and further specify

that those compositions are "in the form of a vaccine" (EA 3). Appellant objects that the examiner's belated grouping of Claims 189-191 exceeded his authority and asks for our commentary (Reply Brief (RB), p. 2).

We may review any question relating to matters affecting the merits of twice rejected claims. 35 U.S.C. § 134; 37 CFR § 1.191(c)(Dec. 22, 2003). Here, however, the issue of whether the examiner exceeded his authority in newly regrouping appellant's twice rejected claims in the Examiner's Answer is moot. First, appellant has agreed to the examiner's belated separate grouping of Claims 189-191 (RB 2). Second, while composition Claims 189-191 further limit (35 U.S.C. § 112, fourth paragraph) the form of the compositions of Claims 186-188, the generic compositions of Claims 186-188 encompass the compositions of dependent Claims 189-191. Third, we may select any one claim from each of appellant's original groupings of claims and decide the appeal as to the grounds of rejection for each grouping based on the claim selected. 37 CFR § 1.192(c)(7). Thus, even presuming appellant's objections are warranted, we may elect to decide the appealed rejections under 35 U.S.C. § 112, first paragraph, of Claims 183, 185, 186, 188, 189 and 191 as a group based on the examiner's rejection of Claim 189 or 191, and the appealed rejections under

35 U.S.C. § 112, first paragraph, of Claims 184, 187 and 190 as a group based on the examiner's rejection of Claim 190.

B. Rejected claims

183. An isolated, MAGE tumor rejection antigen precursor protein, wherein said protein is encoded by a nucleic acid molecule, the complementary sequence of which hybridizes to SEQ ID NO: 8 at 0.1xSSC, 0.1% SDS, wherein said tumor rejection antigen precursor is obtainable from melanoma cells.

184. The isolated tumor rejection antigen precursor protein of claim 183, the amino acid sequence of which comprises the amino acid sequence set forth in SEQ ID NO: 26.

185. The isolated tumor rejection antigen precursor protein of claim 183, wherein said protein is a human protein.

186. Composition comprising the isolated tumor rejection antigen precursor protein of claim 183, and a pharmaceutically appropriate ingredient.

187. Composition comprising the isolated tumor rejection antigen precursor protein of claim 184, and a pharmaceutically appropriate ingredient.

188. Composition comprising the isolated tumor rejection antigen precursor protein of claim 185, and a pharmaceutically appropriate ingredient.

189. The composition of claim 186, in the form of a vaccine.

190. The composition of claim 187, in the form of a vaccine.

191. The composition of claim 188, in the form of a vaccine.

C. Examiner's rejections

The examiner twice rejected appellant's Claims 183-191 under 35 U.S.C. § 112, first paragraph, as not supported by a

specification which, as filed, adequately describes, and/or would have enabled persons skilled in the art to make and use, the full scope of the invention claimed. Based on three groupings of claims, each defining appellant's invention with a different degree of intricacy, the examiner argues that the supporting specification would not have adequately described and/or enabled the full scope of the invention of each group of claims for one or more of the following three deficiencies.

First, the Examiner's Answer for the first time interprets Claims 189-191 as being directed to compositions which are not just vaccines, but vaccines defined on page 309 of the Illustrated Dictionary of Immunology, Cruse and Lewis, CRC Press, Boca Raton, FL, 1994, as follows (EA 4):

> Vaccine: Live attenuated or killed organisms or parts or products from them which contain antigens that can stimulate a specific immune response consisting of protective antibodies and T cell immunity. A vaccine should stimulate a sufficient number of memory T and B lymphocytes to yield effector T cells and antibody-producing B cells from memory cells. It should also be able to stimulate high titers of neutralizing antibodies. Invention [sic, injection?] of a vaccine into a nonimmune subject induces active immunity against the modified pathogens.

Interpreting the compositions of appellant's Claims 189-191 as dictionary-defined vaccines, the examiner relied upon art of record to support his view that appellant's specification would not have

adequately described, or enabled one skilled in the art to make and use, the full scope of the dictionary-defined vaccines to which appellant's claims are said to be drawn.

Second, the examiner argues that the MAGE tumor rejection antigen precursors (hereafter MAGE TRAPS) of Claims 183, 185, 186, 188, 189 and 191 are not adequately described and/or would not have been enabled by appellant's specification. Appellant's claims define MAGE TRAPS solely by reference to melanoma cells from which they were obtained and the polynucleotide sequence SEQ ID NO: 8 to which polynucleotide sequences complementary to polynucleotides encoding the claimed MAGE TRAPS will hybridize at 0.1xSSC, 0.1 % SDS (AB 25, Claim 183). We understand the examiner's position to be that persons skilled in the art would not have believed from appellant's specification that the inventors thereof had possession of the full scope of the inventions appellant claims, and/or that persons skilled in the art would have been able to make and use the same without undue experimentation. Appellant's specification teaches that cytotoxic T lymphocytes (CTLs) target TRA/MHC complexes, i.e., tumor rejection antigens/associated major histocompatibility complex molecules. According to the examiner, the supporting specification does not establish a correlation between the full scope of claimed MAGE TRAPs from which MAGE TRAs

that form TRA/MHC complexes can be derived and the capacity for sequences complementary to polynucleotide sequences which encode the full scope of MAGE TRAPs encompassed by appellant's claims to hybridize to SEQ ID NO: 8 at 0.1xSSC, 0.1 % SDS (EA 6, first two para.; EA 10, para. 4-6; EA 11; EA 12, second para.; EA 15, third full para.; EA 17, para. 4-5; EA 18, first para.; EA 19, first two para.; EA 22, para. 3-4; EA 24, last para.; EA 25, para. 3-5; and EA 26, para. 2-4).

Third, the examiner argues that appellant's specification does not establish a correlation between amino acid sequence SEQ ID NO: 26 in appellant's Claims 184, 187 and 190 and the full scope of claimed MAGE TRAPs from which MAGE TRAs that form target TRA/MHC complexes can be derived. Having established no nexus between either hybridization to polynucleotide sequence SEQ ID NO: 8 or amino acid sequence SEQ ID NO: 26 and the MHC complexing ability of MAGE TRAs derived from the full scope of MAGE TRAPs claimed, appellant's specification does not provide an adequate written description of, and/or would not have enabled persons skilled in the art to make and use, the full scope of MAGE TRAPs appellant's claim for any functional utility the specification suggests.

Discussion

A. Claim interpretation

The examiner concluded that Claims 189-191 are drawn to conventional, dictionary-defined vaccines. The examiner defined all vaccines to which dependent Claims 189-191 are directed, and all vaccines encompassed by composition Claims 186-188 upon which Claims 189-191 respectively depend, in accordance with a dictionary definition of vaccine found on page 309 of the Illustrated Dictionary of Immunology, Cruse and Lewis, CRC Press, Boca Raton, FL, 1994 (EA 4). Using that definition of the term vaccine as the foundation for further action, the examiner presented publications and arguments in support of the view that appellant's specification does not establish that persons skilled in the art reasonably would have understood that applicant possessed all the MAGE TRAPs encompassed by appellant's Claims 183-185 or show that persons skilled in the art would have been able to successfully determine which of the MAGE TRAPs encompassed by Claims 183-185 would be useful in conventional, dictionary-defined vaccines without undue experimentation. The examiner erred in defining the terms of appellant's claims, interpreting the scope and content of the invention claimed, and setting the foundation for his rejections.

The examiner concluded that the compositions to which Claims 186-191 are drawn encompass the vaccines defined on page 309 of the Illustrated Dictionary of Immunology, supra. However, it does not appear that the examiner considered either the language of the claims or the teachings in the specification relating to that claim language. Claims 189-191 are directed to a MAGE TRAP "composition . . . in the form of a vaccine" (BA 25). The use of the phrase "in the form of a vaccine" in Claims 189-191 makes it unclear whether composition Claims 186-191 necessarily are limited to MAGE TRAP compositions which induce immunity in a nonimmune subject or there is a minimum degree or extent to which the compositions must stimulate an immune response consisting of protective antibodies and T cell immunity. In none of the examiner's expositions on the meaning of the term "vaccine" and the patentability of claimed compositions comprising MAGE TRAPS do we find any effort to interpret the meaning of the phrase "composition . . . in the form of a vaccine" or to search the supporting specification for reasons why the inventors used that particular phrase. Rather, the examiner focuses entirely on extrinsic evidence for one contemporary definition of the term "vaccine". Moreover, we find in the examiner's answer and multiple supplements

thereto little or no effort to interpret the scope and content of the invention claimed in light of appellant's disclosure.

Most recently, the Federal Circuit reemphasized how important it is to begin the task of claim interpretation by considering the intrinsic evidence, i.e., the claims, the specification, and the prosecution history. Phillips v. AWH Corp., 415 F.3d 1303, 1316-1320, 75 USPQ2d 1321, 1327-1331, (Fed. Cir. 2005)(en banc). Extrinsic evidence, such as dictionary definitions of terms, should be considered after considering the intrinsic evidence. See Vitronics Corp. V. Conceptronic, Inc., 90 F.3d 1576, 1582-1583, 39 USPQ2d 1573, 1576-77 (Fed. Cir. 1996):

> It is well-settled that, in interpreting . . . [a] claim, we] should look first to the intrinsic evidence of record, i.e., . . . the claims, the specification and . . . the prosecution history. See Markman[v. Westview Instruments, Inc.], 52 F.3d [967,] . . . 979, 34 USPQ2d [1321,] . . . 1329 [(Fed. Cir. 1995)(in banc) aff'd 517 U.S. 370 (1996)]. Such intrinsic evidence is the most significant source of the legally operative meaning of disputed claim language.
>
> First, we look to the words of the claims themselves . . . to define the scope of the . . . invention. . . . Although words in a claim are generally given their ordinary and customary meaning, a patentee may choose to be his own lexicographer and use terms in a manner other than their ordinary meaning, as long as the special definition of the term is clearly stated in the patent specification or file history. . . . .
>
> Thus, second, it is always necessary to review the specification to determine whether the inventor has used any terms in a manner inconsistent with their ordinary meaning.

> The specification acts as a dictionary when it expressly defines terms used in the claims or when it defines terms by implication. Markman, 52 F.3d at 979, 34 USPQ2d at 1330. As we have repeatedly stated, "[c]laims must be read in view of the specification, of which they are a part." Id. At 979, 34 USPQ2d at 1329. The specification contains a written description of the invention which must be clear and complete enough to enable those of ordinary skill in the art to make and use it. Thus, the specification is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term.
>
> Third, the court may also consider the prosecution history . . . .
>
> In most situations, an analysis of the intrinsic evidence alone will resolve any ambiguity in a disputed claim term. In such circumstances, it is improper to rely on extrinsic evidence. See, e.g., Pall Corp. V. Micron Separations, Inc., 66 F.3d 1211, 1216, 36 USPQ2d 1225, 1228 (Fed. Cir. 1995) ("In construing the claims we look to the language of the claims, the specification, and the prosecution history. Extrinsic evidence may also be considered, if needed to assist in determining the meaning or scope of technical terms in the claims.")

Liberally quoting from the opinions in Vitronics and Markman, the Federal Circuit added, Phillips v. AWH Corp., 415 F.3d at 1316-1317, 75 USPQ2d at 1327:

> The Patent and Trademark Office ("PTO") determines the scope of the claims in patent applications not solely on the basis of the claim language, but upon giving claims their broadest reasonable construction "in light of the specification as it would be interpreted by one of ordinary skill in the art." In re Am. Acad. Of Sci. Tech. Ctr., 367 F.3d 1359, 1364 [70 USPQ2d 1827](Fed. Cir. 2004). Indeed, the rules of the PTO require that application claims must "conform to the invention as set forth in the remainder of the specification and the terms and phrases used in the claims

must find clear support or antecedent basis in the description so that the meaning of the terms in the claims may be ascertainable by reference to the description." 37 CFR § 1.75(d)(1). It is therefore entirely appropriate for a court, when conducting claim construction, to rely heavily on the written description for guidance as to the meaning of the claims.

In particular, the Phillips court criticized the significance of dictionaries and treatises as a primary means for defining claim terminology. Phillips v. AWH Corp., 415 F.3d at 1317-1318, 75 USPQ2d at 1330, said:

> [W]hile extrinsic evidence "can shed useful light on the relevant art," we have explained that it is "less significant than the intrinsic record in determining 'the legally operative meaning of claim language.'" C.R. Bard, Inc. v. U.S. Surgical Corp., 388 F.3d 858, 862 [73 USPQ2d 1011] (Fed. Cir. 2004), quoting Vanderlande Indus. Nederland BV v. Int'l Trade Comm'n, 366 F.3d 1311, 1318 [70 USPQ2d 1696] (Fed. Cir. 2004) . . . .
>
> Within the class of extrinsic evidence, the court has observed that dictionaries and treatises can be useful in claim construction. . . . Because dictionaries, and especially technical dictionaries, endeavor to collect the accepted meanings of terms used in various fields of science and technology, those resources have been properly recognized as among the many tools that can assist the court in determining the meaning of particular terminology to those of skill in the art of the invention. . . . .

Phillips v. AWH Corp., 415 F.3d at 1320, 75 USPQ2d at 1332, expressed concern that previously adopted methods for claim interpretation have "placed too much reliance on extrinsic sources such as dictionaries, treatises, and encyclopedias and too little

on intrinsic sources, in particular the specification and prosecution history." The approach to claim interpretation should not require the specification to take a back seat to the dictionary in defining claim terminology. Rather, the specification should govern the use of dictionary definitions as necessary. Phillips v. AWH Corp., 415 F.3d at 1320-1321, 75 USPQ2d at 1332, cautioned:

> Assigning . . . a limited role to the specification, and in particular requiring that any definition of claim language in the specification be express, is inconsistent with our rulings that the specification is "the single best guide to the meaning of a disputed term," and that the specification "acts as a dictionary when it expressly defines terms used in the claims or when it defines terms by implication." Vitronics, 90 F.3d at 1582 . . . .

In this case, the Examiner's Answer first cites and relies upon a dictionary to define the term "vaccine" appearing in appellant's Claims 189-191 and then allows that definition not only to support, but to set the foundation for, the examiner's strongest case for unpatentability thereof under 35 U.S.C. § 112, first paragraph. In so doing, the examiner erred.

Accordingly, we might decline to review the appealed rejections of Claims 189-191 under 35 U.S.C. § 112, first paragraph, and remand the case to the examiner because the examiner interpreted the terms of the claims on appeal, and thus the full scope and content of the claimed subject matter, based primarily on

a dictionary definition of the term "vaccine," seemingly without considering the express language of the claims or significant teachings in the supporting specification. In deciding issues arising under 35 U.S.C. § 112, first paragraph, the specification as a whole must be considered. In re Wright, 866 F.2d 422, 424, 9 USPQ2d 1649, 1651 (Fed. Cir. 1989). Prior to considering whether the invention claimed is adequately described in, or the claimed invention would have been enabled by, appellant's specification as a whole, the full scope and content of the invention claimed must be determined in light of the specification's teaching. Id. Issues involving the patentability of claimed subject matter under 35 U.S.C. § 112, first paragraph (adequate written description and/or enablement), and under 35 U.S.C. § 102/103 (anticipation or obviousness) cannot, and properly should not, be considered until the full scope and content of the claimed subject matter has been determined. In re Moore, 439 F.2d 1232, 169 USPQ 236 (CCPA 1971), instructs at 1235, 169 USPQ at 238, "[T]he claims must be analyzed first in order to determine exactly what subject matter they encompass." Accord In re Angstadt, 537 F.2d 498, 501, 190 USPQ 214, 217 (CCPA 1976). "Before considering the rejections under 35 U.S.C. §§ 103 and 112, we must first decide . . . [what] the claims include within their scope." In re Geerdes, 491 F.2d 1260,

1262, 180 USPQ 789, 791 (CCPA 1974). It is improper to analyze the claimed subject matter and consider the merits of rejections under 35 U.S.C. §§ 103 and 112 "relying on what at best are speculative assumptions as to the meaning of the claims." In re Steele, 305 F.2d 859, 862-863, 134 USPQ 292, 295 (CCPA 1962).

On the other hand, the Federal Circuit has instructed that the mode of claim interpretation used by the courts when litigating issued patents differs from the mode used during prosecution of an application pending in the Patent and Trademark Office. In re Zletz, 893 F.2d 319, 321, 13 USPQ2d 1320, 1321-1322 (Fed. Cir. 1989). Zletz, 893 F.2d at 321, 13 USPQ2d at 1322, instructs that claims of pending applications must be interpreted as broadly as their terms reasonably allow, and there is no reason to read limitations found in the specification into the claims. Nevertheless, Zletz instructed, id. at 321, 13 USPQ2d at 1322, "When applicant states the meaning that the claim terms are intended to have, the claims are examined with that meaning . . . ." In short, whether interpreting the scope and content of subject matter claimed in a patent application pending in the PTO or in an issued patent, "[c]laims must always be read in light of the specification." In re Fout, 675 F.2d 297, 300, 213 USPQ 532, 535

(CCPA 1982). Accord Phillips v. AWH Corp., 415 F.3d at 1316, 75 USPQ2d at 1328.

Here, the examiner appears to have defined the terms, and accordingly the scope and content, of appellant's claims solely by reference to a dictionary definition of the term "vaccine". The examiner appears to have disregarded inconsistent instruction in appellant's specification. Thus, as interpreted by the examiner of the application on appeal, appellant's composition Claims 186-191 are directed to "vaccines" as defined by a dictionary, irrespective of the claim language or the specification's teachings. In so doing, the examiner erred. Nevertheless, due to the length of prosecution in this case, we shall not remand this case to the examiner for remedial claim interpretation.

Appellant's composition Claims 189-191 are drawn to a composition encompassed by Claim 186 "in the form of a vaccine". Claims 186-188 are all directed to compositions comprising an isolated tumor rejection antigen precursor (TRAP) protein encompassed by Claim 183 and a pharmaceutically appropriate ingredient. Thus, appellant claims compositions in the form of a vaccine comprising an isolated TRAP protein and a pharmaceutically appropriate ingredient. For further definition of the claim terminology, we look to appellant's specification.

We find the following passages reproduced from appellant's specification most significant to the task of claim interpretation before us. The specification teaches:

> A class of antigens has been recognized which are presented on the surface of tumor cells and are recognized by cytotoxic T cells, leading to lysis. This class of antigens will be referred to as "tumor rejection antigens" or "TRAs" hereafter. TRAs may or may not elicit antibody responses. The extent to which these antigens have been studied, has been via cytolytic T cell characterization studies, in vitro i.e., the study of the identification of the antigen by a particular cytolytic T cell ("CTL" hereafter) subset. The subset proliferates upon recognition of the presented tumor rejection antigen, and the cells presenting the antigen are lysed. Characterization studies have identified CTL clones which specifically lyse cells expressing the antigens. . . . .

(See col. 2, l. 31-43, of U.S. Patent 5,925,729 ('729), which issued July 20, 1999, from Application 08/142,368, filed May 2, 1994, from which the present application was divided.);

> The gene [which codes for the tumor rejection antigen precursors which are processed to form the presentation tumor rejection antigens] is useful as a source for the isolated and purified tumor rejection antigen precursor and the TRAS themselves, either of which can be used as an agent for treating the cancer for which the antigen is a "marker", as well as in various diagnostic and surveillance approaches to oncology . . . . The tumor rejection antigen precursor may be expressed in cells transfected by the gene, and then used to generate an immune response against a tumor of interest.

('729, col. 3, l. 25-38);

> EXAMPLE 13
>
> . . . This peptide when administered to samples of P0.HTR cells in the presence of CTL cell lines specific to cells

presenting it, led to lysis of the P0.HTR cells, lending support to the view that peptides based on the product expressed by the gene can be used as vaccines.

('729, col. 12, l. 31-36);

EXAMPLE 34

The usefulness of the TRAPs, as well as TRAs derived therefrom, was exemplified by the following.

Exon 3 of mage 1 was shown to transfer expression of antigen E. As a result, it was decided to test whether synthetic peptides derived from this exon 3 could be used to confer sensitivity to anti-E CTL.

To do this, and using standard protocols, cells normally insensitive to anti-E/CTLs were incubated with the synthetic peptides derived from Exon 3.1. Using the CTL lytic assays described supra on P815A, and a peptide concentration of 3 mM, the peptide Glu-Ala-Asp-Pro-Thr-Gly-His-Ser-Tyr was shown to be the best. The assay showed lysis of 30%, indicating conferring of sensitivity to the anti-E CTL.

('729, col. 22, l. 34-47);

As the foregoing discussion makes clear, the sequences code for "tumor rejection antigen precursors" ("TRAPs") which, in turn, are processed into tumor rejection antigens ("TRAs"). Isolated forms of both of these categories are described herein, including specific examples of each. Perhaps the most noteworthy aspect is as vaccines for treating various cancerous conditions. The evidence points to presentation of TRAs on tumor cells, followed by the development of an immune response and deletion of the cells. The examples show that when various TRAs are administered to cells, a CTL response is mounted and presenting cells are deleted. This is behavior characteristic of vaccines, and hence TRAPs, which are processed into TRAs, and the TRAs themselves may be used, either alone or in pharmaceutically appropriate compositions, as vaccines. Similarly, presenting cells may be used in the same manner, either alone or as combined with ingredients to yield pharmaceutical compositions. Additional materials which

> may be used as vaccines include isolated cells which present the TRA molecule on their surface, as well as TRAP fragments, mutated viruses, especially etiolated forms, and transfected bacteria. "Fragments" as used herein refers to peptides which are smaller than the TRA, but which possess the properties required of a vaccine, as discussed supra. Another vaccine comprises or consists of complexes of TRA and HLA molecule. Vaccines of this type described herein may be used preventively, i.e., via administration to a subject in an amount sufficient to prevent onset of a cancerous condition.
>
> The generation of an immune response, be it T-cell or B-cell related, is characteristic of the effect of the presented tumor rejection antigen. With respect to the Bcell response, this involves, inter alia, the generation of antibodies to the TRA, i.e., which specifically bind thereto. In addition, the TRAP molecules are of sufficient size to render them immunogenic, and antibodies which specifically bind thereto are a part of this invention. . . . .

('729, col. 24, l. 25-61); and

> There are therapeutic aspects of this invention as well. The efficacy of administration of effective amounts of TRAPs and TRAs as vaccines has already been discussed supra. Similarly, one may develop the specific CTLs in vitro and then administer these to the subject. Antibodies may be administered, either polyclonal or monoclonal, which specifically bind to cells presenting the TRA of interest. . . . Thus, "targeted" antibody therapy is included herein, as is the application of deletion of the cancerous cells by the use of CTLs.

('729, col. 26, l. 13-25).

Based solely on the claim language and all of the aforementioned teachings in the appellant's specification, we conclude that the compositions of appellant's Claims 186-191 are not limited to dictionary-defined vaccines. Compositions claimed

"in the form of a vaccine" may be vaccines even though they are not dictionary-defined vaccines. The critical question is whether or not the term "vaccine" in the specification is therein defined in accordance with the examiner's strict interpretation of the term vaccine or not.

Citing page 309 of the Illustrated Dictionary of Immunology to conventionally define the term "vaccine" in appellant's claims, the examiner requires appellant's specification to establish that the full scope of the claimed compositions stimulate not only a specific immune response, be it antibody or T-cell related, but an immune response sufficiently strong to neutralize all pathogens in an afflicted subject or induce active immunity in a nonimmune subject. Relying on information disclosed in publications of record to back its unpatentability arguments, the examiner stated that the art shows that "known MAGE molecules exhibit extremely low immunogenicity and initiation of a strong immune response to tumor antigens is [sic, in] vivo is an extremely rare event" (EA 13, sixth para.). More specifically, the examiner argues (EA 14, fourth para.):

> Kirkin et al. (APMIS 106: 665-679, 1998) reviews melanoma-associated antigens recognized by cytotoxic T lymphocytes and notes their genuinely low immunogenicity (see entire document, including Abstract on page 665 and Immunogenicity of tumor cells on pages 673-674). For example,

> "from an immunological point of view, the MAGE antigens represent very good targets for immunotherapy" and yet "so far only one patient has shown an immune response to this group of antigens, suggesting an extremely low immunogenicity of the MAGE antigens" (see page 669, column 2, paragraph 1). . . . .

Next, publications are cited to show that persons skilled in the art had not been able to show any correlation between structure throughout the MAGE family of antigens and the requisite function, i.e., a strong immune response. More specifically, the examiner argues (EA 13, last para., through EA14, third para.):

> In discussing the structure and expression of MAGE family genes, De Plaen et al. (Immunogenetics 40: 360-369, 1994) note: "Throughout the MAGE family . . ., there is considerable conservation of hydrophylic and hydrophobic regions, suggesting that the proteins produced by all these genes may exert very similar function. At the present time, however, there is no indication regarding this function." (See page 367, column 2, paragraph 2).
>
> . . . While the MAGE genes may have the potential to code for antigens that could be targets for specific anti-tumor T lymphocyte responses, such responses would rely upon various regions of the different MAGE proteins contributing peptides that combine with various HLA class I molecules (Page 368, column 1, paragraph 2).
>
> . . . . .
>
> While such efforts may provide the groundwork for determining a MAGE tumor antigen precursor, "it is difficult to predict whether therapeutic success will be achieve [sic], even if a significant increase in anti-tumor cytotoxic lymphocytes is obtained by immunization" (see Boon et al. (Int. J. Cancer 54: 177-180, 1993; see page 178, column 2, paragraph 2).

Relying on his strict interpretation of the scope and content of the subject matter appellant claims, the examiner had basis for finding that "[d]efining human tumor antigen or tumor antigen precursors has not been readily apparent to the skilled artisan" (EA 14-15, bridging para., first sentence). The examiner clarified his position (EA 15, third full para.; emphasis added):

> Here, the specification does not provide sufficient written description of a genus of MAGE tumor rejection antigen precursors based upon the limited disclosure/recitation of one nucleic acid encoding MAGE-1 or upon the limited information (nucleic acids but not cDNA sequences nor amino acid sequences nor isolation of MAGE TRAP protein) on each one of MAGE 1-11 TRAP proteins that can be isolated from melanoma cells. There is insufficient written description of the structure/ sequences of nucleic acids or which complementary . . . [sic] complementary sequence can hybridize to SEQ ID NO: 8 and encode a genus of diverse tumor rejection antigen precursors and, in turn, provide the appropriate structural and functional attributes of a genus of tumor antigen precursors, with distinct structural, expression and functional properties.

The problem with the examiner's argument is that the functional attributes and properties by which the examiner defines and characterizes the scope and content of the vaccines to which appellant's claims are directed are inconsistent with the definitions and characterizations of the claimed compositions in appellant's supporting specification. The examiner defines and characterizes the vaccines and/or compositions in the form of vaccines much more stringently than appellant's specification

defines and characterizes the scope and content of the same subject matter.

For example, referring to the technical dictionary definition of vaccine the examiner concluded that the inventions appellant claims, to the extent they encompass vaccines, are directed to vaccines which must induce a strong immune response in a nonimmune subject, i.e., the vaccines must stimulate an immune response sufficiently strong to neutralize pathogens in an afflicted subject or induce active immunity in a nonimmune subject. However, appellant's specification indicates that the claimed vaccines may or may not involve therapeutic aspects ('729, col. 26, l. 13-25). They may or may not elicit antibody responses ('729, col. 2, l. 31-43). According to appellant's specification, it is enough that a fraction of cells presenting the TRAs are identified and lysed by CTLs ('729, col. 2, l. 13-25; '729, col. 12, l. 31-36 (Example 13)). All that is required of appellant's TRAP vaccines is stimulation of an immune response against a tumor of interest ('729, col. 3, l. 25-38). Example 34 teaches that lysis of 30% of insensitive cells upon which sensitivity to anti-E CTL is said to have been conferred shows anti-E CTL sensitivity indicative of an immune response ('729, col. 22, l. 34-47). Appellant's specification repeatedly states that "generation of an immune

response, be it T-cell or B-cell related, is characteristic of the effect of the presented tumor rejection antigen" ('729, col. 24, l. 54-56). Appellant's specification instructs that evidence of an immune response, e.g., stimulation of a CTL response and deletion of TRA-presenting tumor cells, is behavior characteristic of vaccines, irrespective of its strength ('729, col. 24, l. 31-39).

Accordingly, we conclude that the examiner committed reversible error in requiring appellant's specification to establish that the compositions it claims elicit a strong immune response and induce active immunity to pathogens in a nonimmune subject. Appellant's specification teaches that evidence of an immune response characterizes the vaccines it claims. Citing In re Bundy, 642 F.2d 430, 209 USPQ 48 (CCPA 1981), the Federal Circuit noted in Cross v. Iizuka, 753 F.2d 1040, 1048 n.17, 224 USPQ 739, 746 n.17 (Fed. Cir. 1985):

> Variation in potency . . . is a matter of degree of activity, see Bundy, 642 F.2d at 433, 209 USPQ at 51, but is still indicative of activity. There is no requirement that the compounds have the same degree of activity. Id., 209 USPQ at 51.

In re Bundy, 642 F.2d at 433, 209 USPQ at 51, instructs:

> There is no requirement that all [compounds claimed] have the same degree of activity for each use. What is necessary to satisfy the how-to-use requirement of § 112 is the disclosure of some activity coupled with knowledge as to the use of this activity.

During prosecution of a patent application in the PTO, the examiner must read the application's claims as broadly as their terms reasonably allow. However, the claims should not be read unreasonably in a manner inconsistent with the specification.

B. Burden of proof

1. Enablement

The PTO has the initial burden to show that the full scope of the subject matter appellant claims is not patentable under 35 U.S.C. § 112, first paragraph. In re Marzocchi, 439 F.2d 220, 169 USPQ 367 (CCPA 1971), explained at 223, 169 USPQ at 369:

> It has never been contended that appellants . . . intended only to . . . [claim] a single compound. Accepting, therefore . . . a generic one, its recitation must be taken as an assertion by appellants that all of the "considerable number of compounds" which are included within the generic . . . [claim] would, as a class, be operative to produce the asserted . . . characteristics. The only relevant concern of the Patent Office under these circumstances should be over the truth of any such assertion. The first paragraph of § 112 requires nothing more than objective enablement. How such a teaching is set forth, either by use of illustrative examples or by broad terminology, is of no importance.
>
> As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

Marzocchi added, 439 F.2d at 224, 169 USPQ at 370:

> [I]t is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth of accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure.

The court in Marzocchi was "constrained to conclude that the record before us contains insufficient grounds for questioning the accuracy of appellants' teaching that any [of the compounds claimed] . . . will function to accomplish the asserted result." Id. See also In re Brana, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995), and In re Bundy, 642 F.2d 430, 433, 209 USPQ 48, 51 (CCPA 1981).

Applicants need not know how or why their inventions work to satisfy the requirements of 35 U.S.C. § 112, first paragraph. The Federal Circuit noted in Cross v. Iizuka, 753 F.2d 1040, 1042 n.3, 224 USPQ 739, 741 n.3 (Fed. Cir. 1985):

> [I]t is axiomatic that an inventor need not comprehend the scientific principles on which the practical effectiveness of his invention rests, nor is the inventor's theory or belief as to how his invention works a necessary element in the specification to satisfy the enablement requirement of 35 U.S.C. § 112. Fromson v. Advance Offset Plate, Inc., 720 F.2d 1565, 1570, 219 USPQ 1137, 1140 (Fed. Cir. 1983).

Newman v. Quigg, 877 F.2d 1575, 1581-1582, 11 USPQ2d 1340, 1345 (Fed. Cir. 1989), cert. denied, 495 U.S. 932 (1990), instructs:

> While it is not a requirement of patentability that an inventor correctly set forth, or even know, how or why the invention works, Diamond Rubber Co. v. Consolidated Rubber Tire Co., 220 U.S. 428, 435-36 (1911); Fromson v. Advance Offset Plate, Inc., 720 F.2d 1565, 1570, 219 USPQ 1137, 1140 (Fed. Cir. 1983), neither is the patent applicant relieved of the requirement of teaching how to achieve the claimed result, even if the theory of operation is not correctly explained or even understood. In re Isaacs, 347 F.2d 887, 892, 146 USPQ 193, 197 (CCPA 1965); In re Chilowsky, 229 F.2d 457, 463, 108 USPQ 321, 326 (CCPA 1956).

Correctly interpreting the scope and content of appellant's claims in light of the specification; absolving the specification of any need to explain or understand why appellant found that MAGE TRAPS encoded by a nucleic acid molecule, the complementary sequence of which hybridizes to SEQ ID NO: 8 at 0.1xSSC, 0.1% SDS, induce an immune response; and recognizing the examiner's burden of proof, we now consider the argument that appellant's specification does not show any correlation between structure throughout the MAGE family of antigens and their capacity to induce an immune response. We revisit the evidence in support of this argument (EA 13, last para., through EA14, third para.):

> In discussing the structure and expression of MAGE family genes, De Plaen et al. (Immunogenetics 40: 360-369, 1994) note: "Throughout the MAGE family . . ., there is considerable conservation of hydrophylic and hydrophobic regions, suggesting that the proteins produced by all these genes may

> exert very similar function. At the present time, however, there is no indication regarding this function." (See page 367, column 2, paragraph 2).
>
> . . . While MAGE genes may have the potential to code for antigens that could be targets for specific anti-tumor T lymphocyte responses, such responses would rely upon various regions of the different MAGE proteins contributing peptides that combine with various HLA class I molecules (Page 368, column 1, paragraph 2).
>
> . . . . .
>
> While such efforts may provide the groundwork for determining a MAGE tumor antigen precursor, "it is difficult to predict whether therapeutic success will be achieve [sic], even if a significant increase in anti-tumor cytotoxic lymphocytes is obtained by immunization" (see Boon et al. (Int. J. Cancer 54: 177-180, 1993; see page 178, column 2, paragraph 2).

With the foregoing evidence in mind, we look at the examiner's finding (EA 15, third full para.):

> Here, the specification does not provide sufficient written description of a genus of MAGE tumor rejection antigen precursors based on the limited disclosure/recitation of one nucleic acid encoding MAGE-1 or upon the limited information (nucleic acids but not cDNA sequences nor amino acid sequences nor isolation of MAGE TRAP protein) on each one of MAGE 1-11 TRAP proteins that can be isolated from melanoma cells. There is insufficient written description of the structure/ sequences of nucleic acids or which [of] the complementary sequence[s] can hybridize to SEQ ID NO: 8 and encode a genus of diverse tumor rejection antigen precursors and, in turn, provide the appropriate structural and functional attributes of a genus of tumor antigen precursors, with distinct structural, expression and functional properties.

The references cited by the examiner are said to acknowledge that there is considerable conservation of hydrophylic and hydrophobic regions of the MAGE family of genes, suggesting that the proteins produced by all these genes may exert a very similar function. Nevertheless, De Plaen et al., Immunogenetics, Vol. 40: 360-369 (1994), is cited for its recognition at page 367, col. 2, para. 2, that this very similar function was unknown in 1994. However, in this case we must consider the knowledge and skill in the art as of the March 17, 1997, filing date of Application 08/819,669, to decide the merits of the examiner's rejections under 35 U.S.C. § 112, first paragraph. Moreover, while the examiner relies upon the same article for the inference that "MAGE genes may have the potential to code for antigens that could be targets for specific anti-tumor T lymphocyte responses," the examiner suggests that responses to different HLA class I molecules may rely upon different regions of the different MAGE proteins. The examiner's suggestion, or course, is entitled to no more weight than whatever speculation presented to the contrary.

Ultimately, the examiner relies upon the 1993 Boon publication to support his position that therapeutic success using the full scope of MAGE TRAPs encompassed by appellant's claims would have remained difficult to predict in 1997 "even if a significant

increase in anti-tumor cytotoxic lymphocytes is obtained by immunization" in 1993. The examiner cites column 2, paragraph 2, of Boon, Int. J. Cancer, Vol 54, pages 177-180, 178 (1993), for the following statement:

> While these are exciting prospects, it is difficult to predict whether therapeutic success will be achieved, even if a significant increase in anti-tumor CTL is obtained by immunization. Variants having lost the expression of MAGE-1 may arise and allow the tumor to escape the immune response. Loss of HLA expression has been documented in many tumors and will render them refractory to this therapy . . . . It is hoped that some of the losses in HLA expression will be reversible . . . .

On the other hand, the same 1993 Boon publication states that an immune response is predictable. "Successful immunization should generate a significant increase in these precursors" (Boon 1993, p. 178, col. 2, first full para.). Ultimately, Boon 1993 teaches (Boon 1993, p. 178, col. 2, final para.):

> Prospects will undoubtedly improve if we can attack tumors through several antigens. This should improve the efficiency of the attack against antigenic cells and decrease the probability of resistance due to antigen-loss variants. On this count, we are optimistic. The methods that have led to the identification of a first human gene coding for tumor-rejection antigens should lead soon to the identification of others. This should also considerably expand the cancer patient population that could benefit from specific immunotherapy.

In short, the examiner's arguments that appellant's specification inadequately describes, and would not have enabled

persons skilled in the art to make and use, the full scope of the subject matter claimed are weakly based in fact and law. Appellant's specification teaches, and supports its teaching with examples, that the isolated MAGE TRAP proteins claimed are characterized by their source melanoma cells, their ability to induce an immune response in a nonimmune subject, and sequences which are complementary to the nucleic acid molecules which encode them and will hybridize to SEQ ID NO: 8 at 0.1xSSC, 0.1% SDS. The characterization of the isolated MAGE TRAP proteins claimed in appellant's specification is presumed valid absent evidence which undermines the credibility of the characterization in appellant's specification. The examiner does not criticize the limitation as to source. Nor does the examiner deny that all MAGE TRAPs claimed whose MAGE TRAs have been shown to induce an immune response are in fact encoded by nucleic acid molecules whose complements will hybridize to SEQ ID NO: 8 under the stringent conditions specified in the claims. The examiner's case for both inadequate description and nonenablement appears to stand or fall with the facts that: (1) the specification does not establish that there is a 100% correlation between the ability of polynucleotide sequences which are complementary to polynucleotide sequences which encode MAGE TRAPs to hybridize to SEQ ID NO: 8 and induction of an immune

response by their corresponding MAGE TRAs; (2) evidence in the specification shows that not all polynucleotide sequences which hybridize to SEQ ID NO: 8 are complementary to a polynucleotide sequence which encodes a MAGE TRAP protein whose corresponding MAGE TRAs induce an immune response, and (3) little or no evidence relative to MAGE TRAPs new to the specification supporting the claims of Application 08/819,669 here on appeal has been provided because of cloning difficulties.

Again, the statements made in the specification supporting the claims before us are presumed correct. In re Marzocchi, supra. The examiner has the burden to show otherwise. Here, contrary to the examiner's finding, we find that appellant's specification does establish that there is a correlation between hybridization to SEQ ID NO: 8, polynucleotides which encode MAGE TRAP proteins, and the capacity for the corresponding MAGE TRAs to induce an immune response. That there is evidence in appellant's specification that some experimentation may be required to reduce the full scope of the claimed invention to practice is more indicative of a higher level of guidance and instruction designed to describe and enable one skilled in the art to make and use the full scope of the invention claimed. In re Angstadt, 537 F.2d at 504, 190 USPQ at 219, instructs:

> [T]he PTO has the burden of giving reasons, supported by the record as a whole, why the specification is not enabling. In re Armbruster, 512 F.2d 676, 185 USPQ 152 (CCPA 1975). Showing that the disclosure entails undue experimentation is part of the PTO's initial burden under Armbruster: this court has never held that evidence of the necessity for any experimentation, however slight, is sufficient to require the applicant to prove that the type and amount of experimentation needed is not undue.
>
> . . . Depriving inventors of claims which adequately protect them and limiting them to claims which practically invite appropriation of the invention while avoiding infringement inevitably has the effect of suppressing disclosure. What the dissent seems to be obsessed with is the thought of catalysts which won't work to produce the intended result. Appellants have enabled those in the art to see that this is a real possibility, which is commendable frankness in a disclosure. Without undue experimentation or effort or expense the combinations which do not work will readily be discovered and, of course, nobody will use them and the claims do not cover them. . . . [T]o make everything predictable in advance . . . is impracticable and unreasonable.

We conclude that the examiner has not met his initial burden to prima facie establish the appellant's specification would not have enabled the full scope and content of Claims 183-191 of Application 08/819,669, as of its March 17, 1997, filing date. Accordingly, the appealed final rejections of Claims 183-191 under 35 U.S.C. § 112, first paragraph, for nonenablement are reversed.

2. Description requirement

The examiner relies on substantially the same evidence and arguments in support of his rejections of Claims 183-191 of Application 08/819,669, filed March 17, 1997, under 35 U.S.C.

§ 112, first paragraph, as based on a specification providing an inadequate written description of the subject matter claimed, that he relied upon in support of his rejections for nonenablement. In so doing, it appears that the examiner overlooked our reviewing court's warning in Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991):

> [W]e hereby reaffirm, that 35 USC 112, first paragraph, requires a "written description of the invention" which is separate and distinct from the enablement requirement. The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention.

At the very least, compliance with the enablement requirement of 35 U.S.C. § 112, first paragraph, is a question of law. In re Vaeck, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991). Compliance with its written description requirement is a question of fact. Vas-Cath, Inc. v. Mahurkar, 935 F.2d at 1563, 19 USPQ2d at 1116.

The examiner acknowledges Vas-Cath's warning (EA 12, fourth full para.). However, the examiner appears to have misunderstood the court's statement that the specification conveys to persons skilled in the art that the inventor was in possession of the invention claimed when the skilled artisan recognized that the

inventor invented the subject matter claimed (EA 12, fourth full para.). See In re Gosteli, 872 F.2d 1008, 1002, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Regarding the last sentence of Vas-Cath's warning, Enzo Biochem. Inc. v. Gen-Probe Inc., 323 F.3d 956, 63 USPQ2d 1609 (Fed. Cir. 2002), clarified at 969, 63 USPQ2d 1617:

> That portion of the opinion in Vas-Cath, however, merely states a purpose of the written description requirement, viz., to ensure that the applicant had possession of the invention as of the desired filing date. It does not state that possession alone is always sufficient to meet that requirement. Furthermore, in Lockwood v. American Airlines, Inc., we rejected Lockwood's argument that "all that is necessary to satisfy the description requirement is to show that one is 'in possession' of the invention." 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Rather, we clarified that the written description requirement is satisfied by the patentee's disclosure of "such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention." Id.
>
> . . . Application of the written description . . . is not subsumed by the "possession" inquiry. A showing of "possession" is ancillary to the statutory mandate that "[t]he specification shall contain a written description of the invention," and that requirement is not met if, despite a showing of possession, the specification does not adequately describe the claimed invention. After all . . . one can show possession of an invention by means of an affidavit or declaration during prosecution, as one does in an interference or when one files an affidavit under 37 C.F.R. § 1.131 to antedate a reference. However, such a showing of possession alone does not cure the lack of a written description in the specification, as required by statute.

Perhaps the purpose of the written description requirement is best stated in Reiffin v. Microsoft Corp., 214 F.3d 1342, 1345-46,

54 USPQ2d 1915, 1917 (Fed. Cir. 2000), as follows:

> The purpose of this provision is to ensure that the scope of the right to exclude, as set forth in the claims, does not overreach the scope of the inventor's contribution to the field of art as described in the patent specification.

The adequacy or inadequacy of the written description of the invention claimed varies with the facts in each case. As said in Capon v. Eshhar, 418 F.3d 1349, 1357-1358, 76 USPQ2d 1078, 1084-1085 (Fed. Cir. 2005):

> The descriptive text needed to meet these requirements varies with the nature and scope of the invention at issue, and with the scientific and technical knowledge already in existence. The law must be applied to each invention that enters the patent process, for each patented advance is novel in relationship to the state of the science. Since the law is applied to each invention in view of the state of relevant knowledge, its application will vary with differences in the state of knowledge in the field and differences in the predictability of the science.
>
> . . . In Amgen Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313, 1332 [65 USPQ2d 1385](Fed. Cir. 2003) the court explained further that the written description requirement may be satisfied "if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure." . . . .
>
> The "written description" requirement must be applied in the context of the particular invention and the state of the knowledge. . . . .
>
> The "written description" requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution. . . . .

We found previously herein that the teachings in appellant's specification as a whole, including the representative examples and sequences reported, reasonably would have led persons skilled in the art to believe that there is a correlation between the ability of a complement to a polynucleotide sequence which encodes a MAGE TRA able to induce an immune response in a nonimmunized subject derived from a claimed precursor and the complement's ability to hybridize to SEQ ID NO: 8. The result is not one hundred percent predictable. Nevertheless, we find that the teachings in appellant's specification would have led persons skilled in the art reasonably to expect success using MAGE TRAPs encoded by polynucleotide sequences complementary to polynucleotide sequences which hybridize to SEQ ID NO: 8 to induce an immune response of some kind in a nonimmunized subject. In Capon v. Eshhar, 418 F.3d at 1358-1359, 76 USPQ2d at 1085, the court said (emphasis added):

> It is well recognized that in the "unpredictable" fields of science, it is appropriate to recognize the variability in the science in determining the scope of the coverage to which the inventor is entitled. Such a decision usually focuses on the exemplification in the specification . . . . .
>
> Precedent illustrates that the determination of what is needed to support generic claims to biological subject matter depends on a variety of factors, such as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter. . . . .

> It is not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize a generic invention. See In re Angstadt, 537 F.2d 498, 504 [190 USPQ 214](CCPA 1976)("The examples, both operative and inoperative, are the best guidance this art permits, as far as we can conclude from the record").

Here, we also have significant "other considerations appropriate to the subject matter." Capon v. Eshhar, 418 F.3d at 1358, 76 USPQ2d at 1085. In this case, appellant directed the examiner's attention to Example 9 of the USPTO's Guidelines for Examination of Patent Applications under the 35 U.S.C. § 112, first paragraph, "Written Description" Requirement, 66 Fed. Reg. 1099 (Jan. 5, 2001) ("Guidelines")(Reply Brief, p. 8 and attachment 1 thereto (RB 8 and att. 1)).

Example 9 of the Guidelines deals with a claim to "[a]n isolated nucleic acid that specifically hybridizes under highly stringent conditions to the complement of the sequence set forth in SEQ ID NO: 1" and that encodes a protein having a specified function (RB att 1). The analysis of the example suggests that the claim should be found to have adequate written description because, among other considerations, "highly stringent hybridization conditions . . . yield structurally similar DNAs" (RB att. 1,

pp. 36-37, bridging para.). This reasoning was cited with approval in Enzo Biochem. Inc. v. Gen-Probe Inc., 323 F.3d at 967, 63 USPQ2d at 1615:

> The PTO has . . . provided a[n] . . . example of genus claims to nucleic acids based on their hybridization properties, and has determined that such claims may be adequately described if they hybridize under highly stringent conditions to known sequences because such conditions dictate that all species within the genus will be structurally similar.

The examiner distinguished Example 9 of the Guidelines because the "claimed genus in the instant application still encompasses an enormous number of species with potentially widely diverse properties and describes them structurally simply by hybridization language" (Supplemental Examiner's Answer In Response To Order Returning Undocketed Appeal To Examiner, p. 16, fifth para.). In our view, the examiner has not adequately explained why a different result is warranted here. That is, the examiner has not adequately explained why the hybridization conditions recited in the claim in Example 9 would show structural similarity and therefore possession, but the hybridization conditions recited in the present claims would not.

Furthermore, appellant's specification identifies an amino acid sequence of MAGE TRAPs encompassed by Claims 183-191, and Claims 184, 187, and 190 are limited to MAGE TRAPs comprising that

sequence. The examiner's analysis makes no distinction between the patentability of appellant's claims further defined by amino acid SEQ ID NO: 26 and not. Accordingly, we are forced to conclude that the examiner in this case did not completely analyze the nature and scope of the invention claimed relative to the scientific and technological knowledge in existence at the pertinent time, and accordingly, did not fully consider all evidence material to the patentability of the subject matter defined by appellant's claims.

The court in Capon v. Eshhar, 418 F.3d at 1358, 76 USPQ2d at 1085, instructed:

> See In re Wallach, 378 F.3d 1330, 1333-34 [71 USPQ2d 1939](Fed. Cir. 2004)(an amino acid sequence supports "the entire genus of DNA sequences" that can encode the amino acid sequence because "the state of the art has developed" such that it is a routine matter to convert one to the other) . . . .

Here, the examiner did not consider the extent to which, or the difficulty with which, persons skilled in the art could have identified polynucleotide sequences of the full scope of MAGE TRAPs appellant claims in light of the disclosure of an amino acid sequence of MAGE TRAPs encompassed thereby and polynucleotide SEQ ID NO: 8 to which the complement of the polynuclotide sequences which encode all MAGE TRAPS encompassed by appellant's claims must hybridize under stringent conditions.

The examiner's verbiage in this case cannot serve to replace the comprehensive analysis of the claimed subject matter, the teaching in appellant's specification, the state of the art, and the knowledge and skill of persons skilled in the art at the time this application was filed which is required to satisfy the PTO's burden to establish the unpatentability of the full scope of the claimed subject matter under 35 U.S.C. § 112, first paragraph. Accordingly, we must reverse all the examiner's final rejections here on appeal.

Nevertheless, we are not satisfied that a patent including the claims here on appeal should be granted based on the record presently before us. There are significant patentability issues which appear not to have been raised or even considered by the examiner.

C. Other issues

First, in the array of papers before us, including the appeal brief, examiner's answer, reply brief, two supplemental examiner's answers, and replies to the supplemental examiner's answers and art newly submitted in support thereof, there is a running debate between appellant and the examiner regarding the prior art status of one or more recently published references relied upon by either

appellant or the examiner in support of their respective positions regarding the patentability of the claims before us. The examiner sometimes denies a reference's prior art status. Other times, the examiner relies on a reference's prior art status. Appellant invariably takes the opposing position.

We have reviewed all the art cited by appellant for its evidentiary value in support of the respective positions of appellant and the examiner on the critical issues before us. Post-filing publications are not necessarily worthless and cannot be disregarded as a matter of law. Citing In re Hogan, 559 F.2d 595, 605, 194 USPQ 527, 537 (CCPA 1977), the court in Plant Genetic Systems, *N.V.* v. DeKalb Genetics Corp., 315 F.3d 1335, 65 USPQ 1452 (Fed. Cir. 2003), restated at 1344, 65 USPQ2d at 1459:

> This court has approved use of later publications as evidence of the state of the art existing on the filing date of an application. That approval does not extend, however, to the use of a later . . . publication disclosing a later (1962) existing state of the art in testing an earlier (1953) application for compliance with § 112, first paragraph. The difference may be described as that between the permissible application of later knowledge about art-related facts existing on the filing date and the impermissible application of later knowledge about later art-related facts . . . which did not exist on the filing date.

We have considered all later knowledge of record about art-related facts existing on the filing date of appellant's

application and tried to discard all later knowledge about later art-related facts which did not exist on the filing date of appellant's application. We find little or no evidence which effectively undermines the presumption that appellant's specification is a fair presentation of the state of the art and the knowledge and skill of persons skilled in the art at the time appellant's application was filed. Nor do we find evidence sufficient to show that the examiner has satisfied his burden to establish that appellant's specification would not have adequately described, and/or enabled persons skilled in the art to make and use, the full scope of the invention now claimed, at the time appellant's present application was filed. Moreover, the evidence as a whole appears to support our findings and conclusions herein above.

Second, when the prior art status of a material publication, the publication date of which predates the latest application's filing date but postdates the filing date of an earlier filed application for which benefit is later claimed under 35 U.S.C. § 119 or § 120, is debated, the examiner is generally charged with a duty to determine whether the full scope of the subject matter

the applicant claims is entitled to benefit under 35 U.S.C. § 119 or § 120 of the earlier application's filing date. That determination is particularly significant where, as here, the claims of the latest application are supported by a specification which admittedly contains new matter. To determine whether the full scope of applicant's latest claims is entitled to benefit of an earlier-filed application's filing date, and thus to determine the prior art status of art of record published only before the filing date of the latest application, the examiner must determine whether the specification of the earlier-filed application would have adequately described and enabled one skilled in the art to make and use the full scope of the subject matter later claimed. If, as may or may not be the case here, the earlier filed specifications do not satisfy 35 U.S.C. § 112, first paragraph, for the full scope of the subject matter claimed in the latest filed application, then any intervening reference published more than one year prior to the effective filing date of the latest application may be prior art under 35 U.S.C. § 102(b). See In re Gosteli, 872 F.2d 1008, 1009-1010, 10 USPQ2d 1614, 1616-18 (Fed. Cir. 1989), and In re Scheiber, 587 F.2d 59, 61-62, 199 USPQ 782, 784-85 (CCPA 1978). In this case, the examiner has not determined whether

appellant has perfected its claims for benefit of the filing dates of its earlier-filed applications for the full scope of the subject matter now claimed and antedated all publications disclosing MAGE-1 which were published more than one year prior to the May 2, 1994, filing date of appellant's parent Application 08/142,368. The examiner has not done so because he has not considered whether the specification of grandparent Application 07/807,043, filed December 12, 1991, satisfies all the requirements of 35 U.S.C. § 112, first paragraph, for the full scope of subject matter encompassed by each claim here on appeal as of its December 12, 1991, filing date.

The examiner in this case considered whether the full scope of the subject matter encompassed by the claims now on appeal would have been adequately described in, and enabled by, appellant's parent Application 08/142,368 filed May 2, 1994. However, the examiner appears not to have considered whether the full scope of the subject matter encompassed by the claims now on appeal would have been adequately described in, and enabled by, appellant's grandparent Application 07/807,043, filed December 12, 1991. The claims for benefit under 35 U.S.C. § 120 in this case are important to the patentability of the subject matter defined by the claims on

appeal because human gene MAGE-1, which is said to encode for a MAGE tumor rejection antigen and said to have been expressed by some tumors, is disclosed in intervening references such as Brasseur et al., Int. J. Cancer (Letter to the Editor), Vol. 52, pp. 839-841 (1992), and Boon et al., Int. J. Cancer, Vol. 54, pp. 177-180 (1993). In short, we recommend that the examiner determine whether appellant has perfected its claims for benefit under 35 U.S.C. § 120 and antedated intervening art. The examiner has not determined the full scope and content of prior art applicable to the claimed subject matter here on appeal.

Finally, we presume that the specification of Boon et al., U.S. Patent 5,342,774, which issued August 30, 1994, from grandparent Application 07/807,043, filed December 12, 1991, satisfies all requirements of 35 U.S.C. § 112, first paragraph, for the full scope of the subject matter defined by Claim 4 thereof. Claim 4 of U.S. Patent 5,342,774 reads (emphasis added):

> 4. An isolated nucleic acid molecule which hybridizes to the nucleic acid molecule which codes for MAGE-1 tumor rejection antigen precursor as set forth in SEQ ID NO: 8 under stringent conditions and which codes for a tumor rejection precursor.

Our decision reversing all the appealed final rejections of Claims 183-191 under 35 U.S.C. § 112, first paragraph, appears to be consistent with the presumption that Claim 4 of grandparent

Application 07/807,043, filed December 12, 1991, now U.S. Patent 5,342,774, is directed to patentable subject matter.

Conclusion

Having considered all the evidence and arguments before us, and given appropriate weight thereto, we reverse all the examiner's final rejections of Claims 183-191 of Application 08/819,669 under 35 U.S.C. § 112, first paragraph, and remand this case for further action consistent with the findings, conclusions, and views expressed herein.

REVERSED; REMANDED

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Administrative Patent Judge)
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)
)
SALLY G. LANE) BOARD OF PATENT
Administrative Patent Judge) APPEALS
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